The Newer Antibiotics in Dermatology

FREDERICK G. NOVY, JR., M.D., *Oakland*

SUMMARY

From the experimental and clinical observations published to date it appears that three new antibiotics, polymyxin, chloramphenicol and aureomycin, will prove to be highly efficacious against many of the infectious dermatoses and venereal diseases.

THE antibiotics as they have been developed have all been found to have a wide use in dermatology and syphilology. Penicillin has proved to be specific against many types of infectious cutaneous diseases. Today penicillin is the most active spirocheticidal drug against syphilis. It is the best single form of therapy against all types of this disease. Penicillin is not recommended for use topically because of the danger of sensitizing the patient and thereby precluding its use in more serious systemic conditions. Streptomycin has been found useful in various forms of cutaneous tuberculosis, tularemia, granuloma inguinale and chancroid. It is also of value when used locally but can cause sensitivity. The use of topical tyrothricin has proved successful in many instances of superficial pyogenic infections.

Recently bacitracin has become available. This antibiotic is derived from a strain of Bacillus subtilis. Because of its toxicity it can only be used locally. It is particularly active against Gram-positive streptococci, staphylococci and pneumococci. Meleney and Johnson[7] have found this antibiotic extremely active against various surgical infections. Miller, Slatkin and Johnson[8] felt that it was as effective as penicillin when used topically in such pyogenic infections as impetigo, ecthyma, folliculitis, and infectious eczematoid dermatitis. Contact dermatitis from the use of bacitracin occurs in about 1 per cent of the cases.

In the past two years three new antibiotics have become available for experimental medical use. These are polymyxin, chloramphenicol and aureomycin. The latter two have recently become available for general use. These three new antibiotics have been completely reviewed in an excellent article by Long and his associates.[6]

POLYMYXIN

In May 1947 Benedict and Langlykke[2] reported that sterile filtrates from the Bacillus polymyxa inhibited the growth of various organisms. Stansly, Shepherd and White,[10] working independently, in July 1947 also isolated an antibiotic substance from Bacillus polymyxa. Since that time this substance has been known as polymyxin. The English workers Ainsworth, Brown and Brownlee[1] isolated an antibiotic substance from Bacillus aerosporus Greer and named it aerosporin. This antibiotic is very similar to polymyxin. Their work was reported in August 1947. Polymyxin is a polypeptide or a mixture of polypeptides. It is heat-stable and does not deteriorate when in contact with serum. Experimentally, it has proved extremely active in vitro against Gram-negative bacteria and is primarily bactericidal. Of particular interest in the treatment of cutaneous diseases is the fact that polymyxin is active against Pseudomonas aeruginosa, the organism which frequently produces otitis externa and other stubborn pyogenic infections. Unfortunately this antibiotic is highly nephrotoxic, so that unless this toxicity is overcome the drug will have to be used topically. Because polymyxin is a polypeptide it is not likely to produce sensitivity. For this reason and because of its wide range of antibacterial activity it may well be the ideal topical antibiotic for infections due to Gram-negative organisms.

CHLORAMPHENICOL

Chloramphenicol was isolated from a soil sample taken at Caracas, Venezuela. It is a product of streptomyces. This antibiotic is a crystalline substance which is soluble in water. It does not deteriorate on heating. It is well absorbed by the gastrointestinal tract and serum levels are obtained equal to those produced by parenteral injection. It is rapidly excreted. It is apparently nontoxic when given in therapeutic doses. This drug has been found to be active against a wide range of diseases and is bacteriostatic rather than bactericidal. To date, chloramphenicol has been shown to be highly effective against the rickettsial diseases such as epidemic and endemic typhus, scrub typhus, Rocky Mountain spotted fever and rickettsial pox. Its use in typhoid fever appears to be specific. It is also active against the viruses of psittacosis and lymphogranuloma venereum. This antibotic should prove to be of value in infections due to Gram-negative organisms. As it has been available for only a short time there are no clinical reports on its effectiveness against cutaneous diseases.

AUREOMYCIN

Aureomycin is another antibiotic derived from one of the soil streptomyces (Streptomyces aureofaciens). On culture a golden yellow pigment is produced. Aureomycin is an amorphous hydrochloride, freely soluble in water. It deteriorates rapidly in alkaline solutions and also in human serum. It has an extremely low toxicity and apparently produces no side-reactions. Experimentally, it has been found to be effective against certain Gram-positive and Gram-negative bacteria. It is less useful than penicillin against streptococci, staphylococci and

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pneumococci. It is as effective as chloromycetin against Gram-negative organisms. It has been found to be active against rickettsial infections and also against some of the viral infections.

Braley, and Sanders[3] recently reported local use of a solution of 0.5 per cent aureomycin borate in a number of ophthalmological conditions. They obtained excellent results in infections due to staphylococcus aureus, D. pneumoniae and H. influenzae. They reported on two patients with tuberculosis uveitis and scrofuloderma who were treated with local and intramuscular aureomycin. The response was equal to that which might have been expected had streptomycin been given. Of particular interest are their findings in the treatment of dendritis keratitis due to herpes simplex. Their patients were greatly benefited by using aureomycin locally. If this finding is substantiated, it will means that for the first time there is a specific drug against the virus of herpes simplex and the drug may be of value in cases of herpes zoster.

One patient with pemphigus has been treated at the University of California with aureomycin given orally and intravenously. While the patient was taking the drug no new bullae developed but during this time the old lesions did not heal. When the drug was stopped, new bullae rapidly appeared. Whether this was a natural remission or a remission due to the use of the drug cannot yet be determined.

VENEREAL DISEASES

Lymphogranuloma venereum: Wright, Sanders, Logan, Prigot and Hill[11] have treated, according to their latest report, a total of 35 patients with this disease. The earlier patients in the series were treated with intramuscular aureomycin, the later with oral aureomycin. The investigators believe there have been only two instances of relapse in this group. Their follow-up, however, has not been complete, as they have been able to follow only 14 of the 35 patients. At the time of their report the average time of observation after discontinuance of the use of the drug was eight weeks. The investigators feel that this drug is far superior to any drug previously used in this disease. The results obtained by them will have to be substantiated in the future before the true value of the drug is known.

Granuloma inguinale: Three patients with this disease were treated by Wright and his associates[11] and reported upon in November 1948. The first was treated in April 1948 and the lesions were completely healed by the first part of June. This patient received a total of 2.02 gm. of aureomycin. The second patient had a diagnosis of granuloma inguinale first made in 1942 and received various types of treatment, none of which were effective. In May 1948 aureomycin was started and a total of 75.6 gm. was given. After three weeks the lesions were completely healed and there had been no recurrence up to the time of the report. The third patient had had granuloma inguinale for ten years and during that time had received many kinds of treatment without benefit. Aureomycin was given, 20 mg. daily for 28 days, and the patient was discharged from the hospital with all lesions healed.

In December 1948 Greenblatt and his associates[4] published a second report of the use of aureomycin in granuloma inguinale. They reported on four patients who had previously received streptomycin but had had relapse. (It was stated that about 10 per cent of the patients treated by streptomycin relapse, and that about half of them respond again when retreated with streptomycin.) The patients that were treated with aureomycin were those that were refractory to streptomycin therapy. In one case healing took place in 14½ days, in another in 19 days. In the third patient the lesions had nearly healed at the end of five days of aureomycin by mouth. In the fourth case aureomycin was given orally for five days and at the end of that time the lesions were negative for Donovan bodies; on the ninth day healing was complete. Greenblatt felt that intramuscular use of aureomycin, beside causing local reaction, was not as effective as oral use.

Syphilis: Heilman[5] found in mice infected with relapsing fever that aureomycin by weight was three times as active as penicillin. Also, in experimental Weil's disease in hamsters it was shown that aureomycin was by weight twice as effective as penicillin. From these observations O'Leary, Keirland and Herrell[9] felt justified in using aureomycin in treating two patients with syphilis. These cases were reported in the early part of December 1948. In one case the patient had primary and secondary syphilis. At first 400 mg. of aureomycin was given orally every four hours and the dose was gradually increased until on the fourth day the patient was receiving 750 mg. at each dose. During this treatment the patient received a total of 44.2 gm. At the end of 24 hours there was typical Herxheimer reaction. Darkfield examination became negative for spirochetes in 60 hours, and even 12 hours before this the spirochetes were sluggish and few in number. There was a satisfactory serologic response. At the beginning of treatment the Kahn test showed 256 units and on subsequent tests the number declined; 41 days from the beginning of treatment the reaction was 32 units. In the second case the patient had primary syphilis. Spirochetes were observed on darkfield examination but results of a Kahn test were negative. The patient received 750 mg. every four hours for 15 days; the total dose was 67.5 gm. Results of darkfield examination at the end of 12 hours were positive, but at the end of 16 hours they were negative. At the end of four days the primary lesion was half the original size and in 15 days was entirely healed. During the treatment the Kahn test reaction became positive (8 units) but at the time of the last examination was again negative.

This is an extremely important observation because it may mean that aureomycin is another antibiotic effective against syphilis. Syphilographers have been much concerned of late because they feel that there are developing penicillin-resistant strains

of spirochetes. If this is so, aureomycin may well be the answer.

2938 McClure Street.

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ADDENDUM

Since this paper was written there have been many interesting reports on the use of these antibiotics in dermatology.

Miller[9] and his associates have made a further report on the use of bacitracin in various kinds of pyodermas and have noted continued excellent results. It is important to note that they have continued to find less than 1 per cent sensitivity reactions in their large group of patients.

Aureomycin has been found to be effective in the Kaposi's varicelliform eruption according to the reports of Baer and Miller[2] and those of Bereston and Carliner.[3] One patient with eczema vaccinatum recovered rapidly after the use of aureomycin.[10] The topical use of aureomycin in strength of 0.5 per cent in water has been found to be effective against herpetic stomatitis.[1, 6]

Binder and Stubbs[4] have treated herpes zoster with aureomycin and obtained good results in four cases. There were no residual effects.

A patient with molluscum contagiosum, according to Guy, Jacob and Guy,[7] responded dramatically to aureomycin.

Dermatitis herpetiformis has been treated with aureomycin and the Robinsons[11] feel it more effective than sulfapyridine.

In the treatment of venereal diseases there have been several more reports concerning the use of aureomycin. In lymphogranuloma inguinale the results appear promising. Hill[8] has made an additional report of nine more cases of granuloma inguinale and the response was as satisfactory as it was in the first three cases he reported. Whether this antibiotic will be as effective as streptomycin in this disease will have to be determined after more cases have been reported.

O'Leary and Kierland, at the Mayo Clinic, have continued their work using aureomycin in the treatment of syphilis with good results. O'Leary, at the recent meeting of the American Academy of Dermatology and Syphilology, stated that he felt that aureomycin can do all that penicillin does in syphilis. Rodriques and co-workers[12] used aureomycin in treating 27 patients with early syphilis. All were followed for three months and the investigators felt that results were as satisfactory as with penicillin.

Chloromycetin has also been used in the treatment of syphilis. Romansky, at a recent meeting of the American Academy of Dermatology and Syphilology, reported upon use of the drug in 25 cases. He felt that the results were satisfactory.

Chen, Dienst and Greenblatt reported on one case of chancroid in which results of treatment with aureomycin were satisfactory.

From these preliminary reports the use of these new antibiotics appears most promising, but at this time their exact value in relation to other drugs cannot be stated until larger groups of cases have been followed and reported.

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